OBESITY: A MODERN EPIDEMIC

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ABSTRACT

It has recently become obvious that the prevalence of obesity has been rapidly increasing in the United States, as well as other countries, over the past two decades. This change has involved both sexes, all age ranges and various ethnic groups. The rising prevalence in children and adolescents is of particular concern because of the implications for negative effects on their morbidity and mortality in young adulthood.

Obesity is definitely associated with a relative increase in diabetes, cardiovascular disease, various cancers, respiratory disorders in sleep, gallbladder disease and osteoarthritis. It also has negative effects on a variety of other conditions such as pregnancy complications, menstrual disorders, psychological disorders, and urinary stress incontinence. It is an integral component of the metabolic syndrome, which is emerging as a key constellation of risk factors for cardiovascular disease.

Dealing with this epidemic will require the mobilization of multiple constituencies and allocation of adequate resources. These approaches should be instituted with urgency.

INTRODUCTION

Literally thousands of articles in the scientific press, popular magazines and newspapers have been written about the increased prevalence of obesity in the past few years. The problem has been called an epidemic and compared to the harmful effects of tobacco and alcohol in terms of the extent of its negative impact on the health of the population. Furthermore, as the full extent of the relatively rapid increase in weight in the population has been recognized, the significant involvement of children and adolescents in this change has become obvious. It is interesting to consider why the increase in obesity in the population over the past two decades has suddenly been recognized as so potentially harmful. Undoubtedly the publication of the NHANES data from 1999–2000 by Flegal et al in 2002 (1) was key in bringing this problem

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to the attention of health professionals as well as the public. In addition, the excellent review by Kopelman (2) published in 2000 highlighted many aspects about obesity that were underappreciated, and also stressed obesity as a medical problem with deleterious effects on health. In retrospect there were earlier indications of the increasing prevalence of obesity in the U.S. population in Kuczmarski et al (3) analysis of the NHANES III (1988–1994) survey and the Behavioral Risk Factor Surveillance System (BRFSS) data published in 1999 (4).

In any event, there is no denying the seriousness of the obesity epidemic in 2004 and there is also widespread agreement that it is urgent to develop approaches to both treat those with the disorder, as well as reduce the prevalence of obesity in the population in the future. In this review I will briefly outline how one can measure obesity, describe the prevalence of obesity in various age and ethnic groups, indicate the implications of obesity on mortality and morbidity and analyze the conditions and diseases associated with obesity including the metabolic syndrome. I will indicate other reviews which summarize the metabolic/endocrine milieu accompanying obesity, including the complex array of metabolically active peptides secreted by adipose tissue, and which may play an etiological and/or pathogenic role in development of complications associated with the obese state, as well as the therapeutic options currently available.

MEASUREMENT OF OBESITY

Obesity is characterized by an excess of adipose tissue. There are, however, different types of fat and different locations for fat in the body (2,5). Visceral fat has been shown to be a better indicator of obesity associated disorders than the amount of total fat. The most commonly used measurement for determining obesity is the body mass index (BMI), which is calculated as the weight (kg)/height (m^2) or as the weight (lb)/height (in^2) $\times$ 703. There are reference tables from which one can readily determine the BMI from measurements of the body weight in pounds and the height in inches (6). Although there are some limitations to measuring obesity by the BMI, it is an index that provides a measurable estimate of body fat and is related to the risk of complications associated with obesity (7).

There are alternative measurements of obesity that are useful (8). As an example, the elderly tend to have a shift of fat from peripheral to central sites with a concomitant increase in waist-to-hip ratio. In this population waist circumference alone has been shown to correlate with

obesity related disorders. In fact, this measurement relates closely to the BMI and does reasonably accurately reflect the proportion of intra-abdominal body fat compared to subcutaneous fat and its disease implications (5). Other methods include underwater weighing (hydrodensitometry), dilution methods (hydrometry), dual energy X-ray absorptiometry (DXA), skin fold measurements by calipers, bioimpedance analysis and imaging methods such as computed tomography (CT) and magnetic resonance imaging (MRI). These latter two methods do distinguish between subcutaneous and visceral abdominal adipose tissue and are thus particularly useful for focused research studies. However, at this time they are too costly and complex to use for individual patient's assessment or large scale epidemiologic studies (8).

The National Institute of Health (NIH) published an important document in 1998 entitled "Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults. The evidence report" (9). Table 1 is taken from that publication. This approach is also compatible with that adopted by the World Health Organization (WHO). The normal range for the BMI is 18.5–24.9, while 25.0–29.9 is class (or grade) 1 overweight, 30.0–39.9 is class (or grade) 2 overweight and $\geq$ 40.0 is class (or grade) 3 overweight. These categories correspond to popular descriptions of normal weight, overweight, obesity and morbid or extreme obesity.

PREVALENCE OF OBESITY

Applying the BMI to epidemiological surveys (1) has indicated that approximately 65% of U.S. adults are overweight (35%) (BMI $\geq$ 25) or

TABLE 1. (From Ref 9)*
*Classification of Overweight and Obesity by BMI, Waist Circumference and Associated Disease Risk**

			Disease Risk* Relative to Normal Weight and Waist Circumference	
	BMI (kg/m_2)	Obesity Class	Men $\leq$ 102 cm ($\leq$40 in) Women $\leq$ 88 cm ($\leq$35 in)	>102 cm (>40 in) >88 cm (>35 in)
Underweight	<18.5		—	—
Normal	18.5–24.9		—	—
Overweight	25.0–29.9		Increased	High
Obesity	30.0–34.9	I	High	Very high
	35.0–39.9	II	Very high	Very high
Extreme obesity	$\geq$40	III	Extremely high	Extremely high

*From NHLBI. Clinical guidelines on the identification, evaluation of overweight and obesity in adults. The evidence report. Obesity Research 1998; 6 (Suppl 2); 51(S)–210(S).

obese (BMI $\geq$ 30) (30%). The greatest increases in the past two decades has been in the highest BMI category (extreme or morbid obesity) i.e. BMI $\geq$ 40. The prevalence of extreme obesity is approximately 4.7% of U.S. adults (up from 0.8% in 1960). When one translates these percentages to absolute numbers the scope of the problem becomes obvious (6). Thus approximately 130 million adults 20+ years old are overweight, while nearly one third (approximately 61.3 million people) are obese. As a consequence less than half of U.S. adults have a healthy weight (BMI $\geq$ 18.5 to $<$ 25).

This increase in body weight has steadily increased over the past two decades in both sexes and amongst nearly all racial/ethnic groups (1,6) including non-Hispanic whites, non-Hispanic blacks, and Mexican Americans. Amongst women, obesity and overweight prevalences were highest among non-Hispanic black women. More than half of non-Hispanic black women aged 40 years or older were obese and more than 80% were overweight.

Two very important publications by Ogden et al (10) and Hedley et al (11) have drawn attention to the distressing facts relating to the prevalence and trends in overweight and obesity among U.S. children and adolescents measured in 1976–1980, 1988–1994 and 1999–2000 and updated between 1999 and 2002. The data was derived from the various NHANES studies. Overweight for this population of 2 to 19 year-olds was defined as at, or above, the 95th percentile of the sex-specific BMI for age growth charts. The prevalence of overweight was 15–16% amongst 6 to 19 year-olds in 1999–2000, which represented a marked increase compared to similar measurements made in 1988–1994 (10.5–11.3%). Amongst the youngest group (2 to 5 years old) the overweight prevalence increased from 7.2% to 10.4% over the decade. These trends were exaggerated in non-Hispanic black and Mexican American adolescents (increase in prevalence of more than 10 percentage points between 1988–1994 and 1999–2000), so that more than 23% of adolescents of these ethnic groups were overweight in 1999–2000. Comparing data from 1999–2000 to 2001–2002 showed no indication that the prevalence of obesity amongst adults and overweight amongst children is decreasing (11).

Finally, it is worth noting that data from the Behavioral Risk Factor Surveillance System (BRFSS), which is a cross sectional telephone survey of non-institutionalized adults, conducted between the years 1986 to 2000, indicated that the prevalence of a BMI of 40 or greater quadrupled and the prevalence of a BMI of 50 or greater increased five fold in adults (4,12).

CONSEQUENCES OF OBESITY

Although there have been studies indicating that increasing body weight is associated with a higher mortality (13), this relationship remained controversial until relatively recently. The excellent study by Calle et al (14) has reinforced the conclusions reached in many earlier analyses that indicate that there is a curvilinear relationship in which the risk of death is increased among those with the highest or lowest weights. Calle et al (14) showed in a large prospective study involving more than a million men and women, that the lowest rates of death from all causes were found at BMIs between 23.5 and 24.9 in men and 22.0 and 23.4 in women. Death rates from all causes (cardiovascular, cancer or other diseases) increased throughout the range of moderate and severe overweight for both men and women in all age groups. It is of interest that the risk was greater for whites than for blacks, particularly black women (14). According to recent NIH statistics obese individuals have a 50 to 100% increased risk of death from all causes compared to normal weight individuals (BMI 20–25). Most of the increased risk is due to cardiovascular diseases. Life expectancy of a moderately obese person could be shortened by 2 to 5 years, while morbidly obese men could reduce their life expectancy by almost 13 years (6).

1. Diabetes

Overweight and obesity are known risk factors for diabetes, heart disease, stroke, hypertension, gallbladder disease, osteoarthritis, sleep apnea and some forms of cancer (uterine, breast; colorectal, kidney and gallbladder). Obesity is also associated with high blood cholesterol, pregnancy complications, menstrual irregularities, hirsutism, stress incontinence, psychological disorders including depression and increased risk during surgical procedures (6).

The high prevalence of diabetes in overweight or obese individuals is of particular concern, especially in young adults. As examples, amongst patients diagnosed with type 2 (non-insulin-dependent) diabetes, 67% have a BMI $\geq$ 27, and 46% have a BMI $\geq$ 30 (6). About 70% of diabetes risk in the U.S. can be attributed to excess weight. In the Nurses Cohort Study, the risk of diabetes increased 5 fold for those with a BMI of 25, 28 fold for those with a BMI of 30, and 93 fold for those with a BMI of 35 or greater compared with women with a BMI of less than 21 (15, 16). Similar patterns of increasing prevalence of diabetes with increasing weight have been noted in men. As was mentioned earlier, a waist circumference of $>$ 40 inches increases the risk of diabetes 3–5 fold even after controlling for BMI. In children and

adolescents Type 2 diabetes has been estimated to account for between 8 and 45% of all new cases of diabetes (17).

2. Cardiovascular Disease

The age-adjusted prevalence of hypertension in overweight U.S. adults is 22.1% for men with BMI 25–27; 27% for men with BMI 27–30; 27.7% for women with BMI 25–27 and 32.7% for women with BMI 27–30. These compare with the prevalence of hypertension of approximately 15% in normal weight men and women (6). The effect of hypertension together with other deleterious hemodynamic effects on the heart has resulted in an increase in the development of congestive cardiac failure (CCF) best documented in the Framingham Heart Study. It is of interest that body weight was directly related to the development of CCF independent of other traditional risk factors (18).

Further analysis of the Nurses Cohort Study has also shown that coronary heart disease (CHD), sudden death and arrhythmias have a greater frequency in obese subjects (19). This increase of CHD was 3.6 fold in women with a BMI > 29 compared to those with a BMI of <21. Similar results were derived from the Framingham Study (18).

3. Cancer

A comprehensive review of the relationship of overweight and obesity to cancer has recently been published by Calle and Kaaks (8). In this presentation I will only highlight several of the important associations. Thus the relative risk (RR) of colorectal cancer in obese individuals is 1.5–2.0 in men and 1.2–1.5 in women. The data regarding breast cancer has been confirmed in several studies indicating that obese postmenopausal women were at increased risk to develop breast cancer by 30–50% (19a). Furthermore, adult weight gain has been associated with a larger increase in risk of postmenopausal breast cancer than the absolute BMI. Obesity also carries with it several additional negative prognostic implications in women with breast cancer, including reduced likelihood of survival and increased likelihood of recurrence in both pre- and postmenopausal women; very obese women (BMI ≥ 40.0) have breast cancer death rates 3 fold higher than normal weight women.

The initial malignancy whose prevalence was related to obesity was endometrial cancer. Many studies have shown an almost linear increase in the risk (2–3.5 fold) in endometrial cancer with increasing BMI (20). Other cancers such as renal-cell cancer (1.5–3.0 $\times$ higher) and adenocarcinoma of the esophagus (2.0–3.0 $\times$ higher) also have a higher risk in obesity. It is probable that with further epidemiological studies, in-

creases in pancreatic, hepatocellular and gallbladder carcinoma, as well as adenocarcinoma of the gastric cardia, will be linked to obesity (8).

In summary, it is estimated that overweight and obesity underlie approximately 90,000 deaths from cancer per year, an indication of how serious this epidemic is in terms of increasing morbidity and mortality in the population. Prevention of overweight and obesity could thus significantly reduce the occurrence of cancer in both men and women as it is estimated that this condition could account for 14% of cancer deaths among men and 20% among women (6).

4. Sleep-Breathing Abnormalities

Breathing problems during sleep are a common consequence of obesity. For example, it is not uncommon for some obese men to have low oxygen saturation during REM sleep while their awake arterial gases are normal (21). A minority of individuals progress to the sleep apnea syndrome (22). In the Swedish Obesity Study, over 50% of the men and 33% of the women with a BMI >35 reported snoring and sleep apnea (23). These changes during sleep seem to carry an increased risk of myocardial infarction and stroke (24).

OVERWEIGHT AND OBESITY IN CHILDREN AND ADOLESCENTS

The rapid increase in obesity in children and adolescents has very troublesome implications in terms of premature mortality and significant morbidity in young people. As an example, Dietz (17) has drawn attention to the tripling of obesity and obesity-associated hospital discharge rates amongst children 6–17 years of age. Approximately 60% of overweight children and adolescents have at least one additional risk factor for cardiovascular disease, such as hypertension, hyperlipidemia or insulin resistance. More than 25% have two or more of these risk factors. Type 2 diabetes has recently been estimated to account for between 8–45% of all new cases of diabetes in children and adolescents. The potential for the development of renal failure, impaired vision, cardiovascular and cerebrovascular disease and the neurological complications of diabetes after fifteen to twenty years, when these individuals are young adults, indicates the incredibly serious implications of this epidemic.

METABOLIC SYNDROME

This syndrome (obesity, high fasting triglycerides, impaired glucose tolerance, hypertension, and low high density lipoprotein) has been

widely studied in adults. Its prevalence in adults is approximately 20% of individuals ≥20 years of age and 40% of the population >40 years of age (25). This syndrome has a high predictive value for the development of diabetes and cardiovascular disease.

It is thus of great concern that this syndrome is being diagnosed in adolescents in increasing numbers. Thus Duncan et al (26) have shown a significant increase in this syndrome in adolescents over the past decade (4.2% in 1988–1992 to 6.4% in 1999–2000). Moreover, the syndrome was found in 32.1% of overweight adolescents (BMI ≥95th percentile for age and sex). These authors extrapolate that there may be more than 2 million U.S. adolescents with this syndrome.

SUMMARY

In this short review I have not dealt with the etiology of obesity, the causes of the obesity epidemic, nor strategies for its prevention and treatment. These are major areas being currently studied and they require the involvement and commitment of the public, our government, health care professionals across all disciplines, as well as scientists and pharmaceutical companies. Only in this way will we be able to mitigate the human and financial implications of this looming catastrophe.

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DISCUSSION

DuBose, Winston-Salem: Arthur, I'm sure this question begs the obvious, but what's the explanation; is it gluttony, is it lack of exercise, is it that during this same decade, the American Heart Association was recommending a heart-healthy diet. Is it where we eat, is it what we eat? What are the explanations?

Rubenstein, Philadelphia: Unfortunately there is no easy answer to this question. It is probably a combination of many things. Unfortunately I don't have time to answer this in detail, but the data at the moment indicates there are major changes in the population in terms of less physical activity and greater caloric intake. And underlying each of these changes is a variety of reasons. It probably involves the way we live, where we live, how we go to school, watching television, use of computers, fast foods, and economic issues related to cost of food and its availability. Every one of these is important, and there is no simple answer to this except that each of those needs to be dealt with in its own right.

DuPont, Houston: One comment and then a question. As we grow older we change our body organization. We atrophy peripherally and with truncal obesity and our BMI's look fine. Does this limit the value of the BMI? My real question relates to the challenges, not in diagnosis, but in management of obesity. I'm not sure where we are headed with it. Identifying a problem is only getting it started, and I know of no innovative ways to approach this thing, because ultimately we have to change behavior. We've been massively unsuccessful in virtually all areas requiring change in behavior. Is there some tricks here that we're going to be successful with?

Rubenstein: The answers to your questions are complicated. There are adjustments to BMI that can be made with age, and there are also simple measurements of waist circumference that relate well in older aged people to medical disorders. We need to start thinking about this problem in various ways including weight and height, but not exclusively with these measurements, because each metric has a relationship to a disease that is worthwhile knowing. Your question regarding behavior modification is right on. We have been unsuccessful as a community in terms of behavioral modification, but there are studies in more selected populations showing that one can achieve changes if one has the will and effort to do so. Tobacco use is a successful example that is so important. People were pessimistic about decreasing smoking 20–30 years ago, but the data in this country at this time indicates substantial success. So we need to really think, starting in children about changing life style in a major way, which, as this data indicates, we really have a major incentive to do. And in there lies the importance of everyone recognizing this problem.

Stevenson, Stanford: Arthur, thank you for pointing out one of the major pediatrics problems that we are confronting right now. I'd like to bring to people's attention the fact that we see obesity in the babies. Although preterm birth remains a very prevalent in neonatology, we are also seeing an epidemic of very large babies. Some infant obesity is related to the gestational diabetes; some of it is related to maternal obesity. The metabolic circumstances responsible for the obesity in the offspring of obese women are not well understood, but the impact is huge, and very similar to the graphs that you showed. If we have infants who get to be heavier than 4 kg, the typical adult woman's pelvis is not engineered by nature to deliver in every case infants over that size safely. Birth trauma is common, including death, and occurs as babies get bigger, independent of the overall health of the people. Moreover, we are probably programming these babies for altered ways in which they are going to handle fuels later in life. So I think this is a huge problem, which is encountered right at the time of birth in the offspring of very large people.

Rubenstein: That's absolutely right, and you know there's a lot of evidence that what

is laid down in fetal development and in the few months after birth, is very difficult to reverse at later ages. For example, the number of fat cells that are programmed in early years is difficult to change in adulthood. So, yes, the problem goes all the way back to pregnancy as you point out.

Barondess, New York: Thank you Arthur for a clear and powerful presentation. There are issues here and lessons we can learn from the social psychologists, who studied in some depth the way people relate to food. I, for example, was trained by my mother to clean my plate. I may not be the only one here, who had that kind of training. It's extraordinarily powerful and persists through life. The idea that it's a moral question whether you finish the amount of food someone else has put on your plate bears, I suggest, some consideration. Some of the studies in the social psychology of eating have demonstrated that people who have ever been obese eat in response to different kinds of cues from the way people who have never been obese eat; people who have never been obese stop eating when they've had enough. People who have ever been obese stop eating when all the food is gone. We are surrounded endlessly by invitations to think about food, and to begin what used to be called the cerebral phase of digestion; endless advertisements, endless invitations to think about food, endless pictures to get your juices going. And I think the clinical and epidemiological communities could with benefit make common cause with these studies and the social psychology of eating.

Rubenstein: Well you point out a whole range of issues, each of which is important in their own right. But it has been shown for example that advertising food to children just to pick out one of them, has a big impact. This is not surprising and is the reason why advertisers influence what children choose to eat, how much, and so on. No one really at this time advertises the importance of exercise, although that's beginning to be done as we recognize its importance. So each of these need behavioral, psychological, social, and economic changes because we have a challenge that involves all kinds of issues in the community.